



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,313	06/03/2002	Michael Hallek	50125/044001	5985
21559	7590	10/18/2006	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			CHEN, STACY BROWN	
			ART UNIT	PAPER NUMBER
			1648	
DATE MAILED: 10/18/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/031,313

Applicant(s)

HALLEK ET AL.

Examiner

Stacy B. Chen

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 91 and 94-100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 91 and 94-98 is/are rejected.
- 7) ☒ Claim(s) 98 and 100 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 31, 2006 has been entered. Claims 91 and 94-100 are pending and under examination.

The rejection of claims 88, 90, 91 and 94-98 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is moot with respect to cancelled claims 88 and 90, and withdrawn with respect to claims 91 and 94-98 in view of Applicant's persuasive arguments.

Claims Summary

The claims are drawn to a method for reducing the antigenicity of an infectious AAV particle. The method comprises introducing at least one modification into AAV VP1, VP2 or VP3, wherein the modification brings about a reduction in the antigenicity of the AAV relative to the wild-type AAV. The modification is located directly adjacent to at least one amino acid in a sequence selected from the group consisting of SEQ ID NO: 2-9. The sequences correspond to the exposed sites of the VP3 loops (page 12, lines 4-12). In new claims 99 and 100, the modification is located directly adjacent to at least one amino acid in SEQ ID NO: 8 and SEQ ID NO: 9, respectively.

Art Unit: 1648

Specifically, the modification is based on a covalent or noncovalent linkage to the structural protein of one or more compound(s) selected from the group consisting of biotin, a mono- or oligosaccharide, a hydroxide group, a Fab fragment, and one or more amino acid(s) or amino acid sequence(s). The modification may be the insertion of a protein or a peptide into VP1, VP2 or VP3. The modification may be a mutation selected from the group consisting of a point mutation, a mutation of more than one amino acid, one or more deletions, one or more insertions, and a combination of these mutations.

Claim Rejections - 35 USC § 102

Claims 91 and 94-98 are rejected under 35 U.S.C. 102(b) as being anticipated by Mamounas *et al.* (WO 97/38723, herein, "Mamounas"), evidenced by Rutledge *et al.* (*Journal of Virology*, 1998, 72(1):309-319, "Rutledge"). The claims are summarized above.

Mamounas discloses a capsid protein (structural protein) of AAV-2 that has been deleted (modified) in the VP1 or VP3 region (Example 1, pages 60-61, bridging paragraph, and page 67, part C). The deletion results in reduced specificity of the virus for the AAV receptor (page 4, lines 22-26), which is a reduction of the antigenicity of the virus for its natural receptor. Mamounas modifications of the VP1, VP2 and VP3 genes include the end of the AAV capsid gene open reading frame, and the start codon of the individual capsid genes (page 67, lines 13-22). Anti-CD34 scFv sequence was ligated to the 5' end of the VP1, VP2, and VP3 sequences using HindIII and NotI sites (page 67, lines 21-26), thus qualifying as a further modification in addition to the deletion(s) in the VP 1 and/or VP3 region.

Art Unit: 1648

Mamounas also teaches deleting a region of the VP1 or VP3 region and inserting a targeting ligand, which is an additional modification (page 4, lines 28-31). Antibodies, such as single chain variable region fragments, biotin, poly-L-lysine, transferrin, and other proteins are contemplated by Mamounas for integration into the VP regions (pages 26, 27 and 30-32). Specifically, Mamounas discloses the preferred expression sites in the AAV vectors at amino acids 26-34 of VP1 and amino acids 239-244 of VP3 (page 4, lines 30-31, and Table 1, Mutation D4). Amino acids 239-244 of AAV VP3 overlap with Applicant's SEQ ID NO: 4 as shown below:

Mamounas' insertion in region 239-244: YLYYLS (see sequence in Rutledge, Figure 4B)

Applicant's insertion in SEQ ID NO: 4: YYLSRNTNTPS

(Rutledge, page 316, Figure 4B, arrow indicating start of VP3 with Met; start with Met as amino acid 1 of VP3, then count to amino acid 239). Therefore, Mamounas teaches an insertion directly adjacent to an amino acid within SEQ ID NO: 4, as required by instant claims 91 and 94-98.

Conclusion

Claims 99 and 100 are free of the prior art of record. Claims 99 and 100 are objected to for depending from rejected claim 91.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

Art Unit: 1648

system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 10/11/06
STACY B. CHEN
PRIMARY EXAMINER